**CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY**
**DEPARTMENT OF PESTICIDE REGULATION**
**MEDICAL TOXICOLOGY BRANCH**

# SUMMARY OF TOXICOLOGY DATA
# ALKYL AMINE HYDROCHLORIDE
# (Cosan 635 Active)

**Chemical Code # 001122, Tolerance # 50543**
**SB 950 # 403**

**Original: September 6, 2002**

## I. DATA GAP STATUS

| | |
|---|---|
| **Chronic toxicity, rat:** | Data gap, no study submitted. |
| Subchronic toxicity, dermal | No adverse systemic effect but dermal irritation. |
| **Chronic toxicity, dog:** | Data gap, no study submitted |
| **Oncogenicity, rat:** | Data gap, no study submitted |
| **Oncogenicity, mouse:** | Data gap, no study submitted |
| **Reproduction, rat:** | Data gap, no study submitted. |
| **Teratology, rat:** | No data gap, no adverse effect. |
| **Teratology, rabbit:** | Data gap, no study submitted. |
| **Gene mutation:** | No data gap, no adverse effect |
| **Chromosome effects:** | No data gap, no adverse effect |
| **DNA damage:** | No data gap, no adverse effect |
| **Neurotoxicity:** | Not required at this time |

---

Toxicology one-liners are attached.

All record numbers through 115626 were examined.

** indicates an acceptable study.

File name: T020906
Original: September 6, 2002

These pages contain summaries only. Individual worksheets may contain additional effects.

## CHRONIC TOXICITY, RAT

Subchronic:

**** 50543 - 007 115620** Naas, D. J. "90-Day Dermal Study in Rats with Alkyl Amine Hydrochloride." ( WIL Research Laboratories, Inc., WIL-159007, December 19, 1990.) Alkyl Amine Hydrochloride (identified as Nuosept 635-W, assumed 100% for dose preparation) was applied at doses of 0 (deionized water), 50, 125, or 250 mg/kg once daily for 6 hours, 5 days/week for thirteen weeks, to the shaved dorsal skin (20 - 25% of body surface) of 15 Crl:CD®BR rats/sex/group. Treated area was occluded and volumes were 5 ml/kg. Total number of applications were 65, 66 or 67. Total body weight for high dose males was significantly reduced, being 13% below control at termination. The major clinical effects were related to dermal irritation, including vocalization, writhing, abnormal posture and hyper-reactivity in all treated groups at the time of dosing, presumed to be related to pain. Daily scores (1 - 4), taken before dosing, increased with dose for erythema and edema. Also, the observation of desquamation was found in all treated animals. The incidence of fissuring in males increased from 9/15 at 50 mg/kg to 15/15 at 125 mg/kg. All females at all doses exhibited fissuring on occasion. Scabbing was seen at some observation time in all treated groups of females and at 125 mg/kg and 250 mg/kg in males. Females showed more severe skin irritation than males. Dermal lesions in histopathology included acantholysis, hyperkeratosis, suppurative inflammation and ulceration for mid and high-dose groups, both sexes. Adrenal weights were increased (absolute and relative) in females at 125 and 250 mg/kg and relative weights in males at 250 mg/kg. There were histological findings and the increase was attributed to the stress of dosing. Systemic NOEL = 125 mg/kg (male body weight) Dermal NOEL $\leq$ 50 mg/kg (irritation seen in all treated groups). Adverse for dermal irritation. ACCEPTABLE. (Kishiyama and Gee, 9/5/02).

50543 - 006 115619 Naas, D. J. "Three Week Dermal Study in Rats with Alkyl Amine Hydrochloride." ( WIL Research Laboratories, Inc., WIL-159004, September 27, 1990.) Alkyl Amine Hydrochloride (lot 190-47, 100%) was applied to the shaved dorsal skin of 5 Crl:CD®BR rats/sex/group at doses of 0 (deionized water), 125, 250, 500, or 1000 mg/kg once daily for 6 hours, 5 days/week for three weeks (15 applications). Doses of 125, 250 and 500 were applied as a suspension in water under occlusive dressing to shaved skin. The high dose was applied as a paste with the test material moistened with 0.4 - 0.5 ml of water before application. Due to the anticipated irritation, application was alternated from side to side on a daily basis. Dermal irritation intensity and severity of the treated skin was time and dose related with the effects being graded as 4 at times for edema in all groups of females and at 250 mg/kg and higher in males and females from erythema and edema. Effects in females were, therefore, considered more severe than in males. There was some evidence of dermal healing for the low dose group towards the end of the study. Other dermal effects noted were desquamation (all doses), eschar (all doses of females), necrosis (250 and higher in females), exfoliation and scabbing. Food consumption was reduced at 500 and 1000 mg/kg in males. Body weight gain was reduced at all dosages for males (very slight at 125 mg/kg), and total body weight was significantly reduced for the three highest dose groups for males. Body weight gain was reduced for the three highest dose groups of females but total body weights were not significantly different. No clinical chemistry, hematology or histopathology were conducted. The purpose of the study was as a range-finding study for a 90-day dermal study. Dermal NOEL $\leq$ 125 mg/kg/day. Systemic NOEL = 125 mg/kg/day. SUPPLEMENTAL DATA. (Kishiyama and Gee, 9/5/02).

## CHRONIC TOXICITY, DOG

No study submitted.

## ONCOGENICITY, RAT

No study submitted

## ONCOGENICITY, MOUSE

No study submitted

## REPRODUCTION, RAT

No study submitted.

## TERATOLOGY, RAT

** 50543 - 008 115622 Nemec, M. D. "A Developmental Toxicity Study of Alkyl Amine Hydrochloride in Rats." ( WIL Research Laboratories, Inc., WIL-152002, May 22, 1990.) Alkyl Amine Hydrochloride (lot 190-47, 100%) was administered via gavage at doses of 0 (0.5% aqueous methyl cellulose), 25, 75, or 150 mg/kg/day in 10 ml/kg/day during gestation days 6-15 to 25 mated female Crl:CD®BR rats/group. Four deaths were observed for the high dose-group, considered due to treatment. Clinical effects at the high dose included yellow staining of the anogenital and urogenital area, red material and staining around forelimbs, red material around nose and mouth, increased salivation, abdominal hair loss, decreased defecation and urination, irregular respiration and reduced food consumption and body weight. Also, a dose related incidence of rales was observed (0/0 in controls, 4/4, 17/13 and 48/13 with increasing dose. Maternal NOEL = 25 mg/kg/day (slight affects on clinical signs, food consumption and body weight at 75 mg/kg, mortality and clinical signs at 150 mg/kg/day). Fetal body weight was lower and post implantation loss increased for the high dose group. Developmental NOEL = 75 mg/kg/day. ACCEPTABLE. (Kishiyama and Gee, 9/4/02).

50543 - 009 115623 Nemec, M. D. "A Range-Finding Developmental Toxicity Study of Alkyl Amine Hydrochloride in Rats." (WIL Research Laboratories, Inc., WIL-152001, May 2, 1990.) Alkyl Amine Hydrochloride (lot 190-47, 100%) was administered via gavage at doses of 0 (0.5% aqueous methyl cellulose), 25, 50, 100, 200 or 300 mg/kg/day in 10 ml/kg during gestation days 6-15 to 8 mated female Sprague Dawley Crl:CD®BR rats/group. There were three deaths at 200 mg/kg/day and four deaths at 300 mg/kg/day, one due to intubation error. The incidences of clinical signs were increased at the two highest doses: dried yellow staining and wet red material urogenital area, dried red material on forelimbs and around nose, mouth and eyes, dehydration, rales, labored respiration, gasping, lacrimation, clear nasal discharge, soft stools, decreased urination and defecation, salivation, reduced food consumption and lower body weight. Maternal NOEL = 100 mg/kg. Mean fetal weight was lower and post implantation loss (early resorptions) were reported for the 200 and 300 mg/kg groups. Despite the increase in resorption, mean litter size was not affected, being similar to control or higher, due to high number of implantation sites and corpora lutea in these two groups. Developmental NOEL = 100 mg/kg. Supplemental data. (Kishiyama and Gee, 9/4/02).

## TERATOLOGY, RABBIT

No study submitted.

## GENE MUTATION

** 50543 - 010 115624 San, R. H. C. and Kruel, C. "*Salmonella*/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test) with a Confirmatory Assay." (Microbiological Associates, Inc., Laboratory Study Number T8767-501014, 7/17/89). Cosan 635 Active (lot 190-24-1, 100%) was tested at concentrations ranging from 1 to 10,000 : g/plate with microsomal enzymes (S9 Mix) and from 0.3 to 667 : g/plate without S9 Mix. Vehicle was 100% ethanol. There were triplicate plates per concentration per trial. The test was repeated. No concentration related increase in revertants was reported. ACCEPTABLE (Kishiyama and Gee, 9/3/02)

## CHROMOSOME EFFECTS

** 50543 - 010 115625 Putman, D. L. and Morris, M. J. "Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells." (Microbiological Associates, Inc., Laboratory Study Number T8767.337, 08/10/89.) Cosan 635 Active (lot 190-24-1, 100%) was evaluated at concentrations of 0 (ethanol), 1.5, 3, 6, 12 and 18 : g/ml with and without metabolic activation (S-9 Mix), using Chinese hamster ovary cells for induction of chromosome aberrations. Exposure times were 2 (with S9 Mix) and 16 hours (without S9 Mix) with a harvest time of 12 hours with activation and 18 hours without activation. Concentrations and harvest times were based on a preliminary study of cell cycle progression and mitotic indices up to 2000 : g/ml. Both 12 and 18 : g/ml were cytotoxic in the main study. No increases in chromosomal aberrations were reported to the limit of cytotoxcicity. Positive controls were functional. ACCEPTABLE. (Kishiyama and Gee, 9/3/02)

## DNA DAMAGE

** 50543 - 010 115626 Curren, R. D. "Unscheduled DNA Synthesis in Rat Primary Hepatocytes." (Microbiological Associates, Inc., Laboratory Study Number T8767.380, 07/20/89.) Cosan 635 Active (lot 190-24-1, 100%) was tested at concentrations of 0 (ethanol), 0.6, 2, 6, 10, 15 and 20 : g/ml with adult male rat (Fischer 344) hepatocytes for 18 - 20 hours of exposure. Cytotoxicity was measured by release of lactic acid dehydrogenase as measured in triplicate plates in parallel with the treated, triplicate plates. The positive control was functional. There was no significant increase mean net nuclear counts as measured by autoradiography. ACCEPTABLE. (Kishiyama and Gee, 9/3/02)

.

## NEUROTOXICITY

Not required at this time.